REMARKS

Reconsideration of the application is requested in view of the amendment to the claims and the remarks presented herein.

The claims in the application are claims 1, 2, 4 to 6 and 10 to 31, all other claims having been cancelled. Applicants paid for 22 claims originally and Applicants are submitting PTO form 2038 for $250 for the addition 5 claims.

Applicants are submitting replacement drawings with the English translations of the titles and axes.

With respect to the objections to the claims, the dependency of claim 13 has been corrected and "A" has been changed to "The" in the dependent claims.

Claim 13 has been amended to refer to the trademarks WHITEPSOL ® and SUPPOCIRE ®. As indicated in the specification WHITEPSOL is a solid semi-synthetic glyceride sold by Condea Chemie Gmbh (Germany) and Suppocire a semi-synthetic glyceride sold by Gattefosse (France) and claim 20 has been clarified to overcome the 35 USC 112, second paragraph rejection.

Claims 1 to 9, 14 and 15 were rejected under 35 USC 102 as being anticipated by the Guittard et al patent which the Examiner states teaches

pharmaceutical compositions of oxybutynin alone or with other drugs to treat incontinency.

Applicants traverse this ground of rejection as the Guittard et al patent document does not teach Applicants' invention which is directed to active formulations intended for adminstration vaginally or rectally because these routes of adminstration allow a steady release of the active ingredient over a very long set of time (until 36 hours) with peaks of maximal resorption culminating between 6 and 8 hours after administration. Moreover, these routes of administration not only allow an extended period of release but with the certainty that the production of the noxious des ethyl metabolite does not occur. This metabolite is a strong atropinic derivative which is responsible for the many side-effects linked to the oral administration of oxybutynin. In contrast thereof, the present formulations such as Ditropan ® are defined by a very short upset of the resorption giving rise to very high blood level after 30 min. after administration, to last for about 4 to 6 hours. Moreover, the amounts of des ethyl metabolite as shown in table 2 are very low in comparison in human patients or even nonexistent during the whole duration of the action, contrarily to the oral administration of oxybutynin which produces significant amounts of des ethyl metabolite.

The Guittard's patent cited a ratio of des ethyl metabolite to oxybutynin of 0.178 that means that for each mg of oxybutynin, 0.178 mg of des ethyl metabolite is produced which is quite sufficient to produce atropinic side effects. In addition,

in accordance with the disclosure of the Guittard's patent, the des ethyl metabolite is a long lasting ingredient and the persistence of such compound is over 12 hours. The Guittard's patent relates only to various formulations intended for oral administration allowing a controlled release of the active ingredient using coated and wrapped pharmaceutical compositions.

Moreover, this patent discloses as formulation allowing a controlled or long lasting release of the active ingredient, an osmotic formulation wherein the active ingredient is release using as osmotic agent such as 50 to 100 mg of sodium chloride. Such a formulation could not be compatible with the vaginal or rectal administration without the risk of painful side effects. Also, Guittard's patent discloses the production of multi-layer formulations using a layer of hydrogel and a layer of active ingredient. The layer of hydrogel includes small amounts of ferric oxide and such an ingredient could not be suitable for vaginal or rectal administration because it will retain or adsorb the active ingredient and will limit the percentage or released active ingredient.

Another kind of formulation disclosed in the Guittard's patent, is a system of dispensation in which the wall of the tablets are of the semi-permeable kind. That means that the wall is semi permeable to the inlet of an external fluid and impermeable to the outlet of oxybutynin. The system has nothing in common with the present formulation which does not need any wrapping in a membrane. In a vaginal or rectal supposition, the mass has to progressively melt at the body

temperature allowing a somewhat delayed release and a long lasting release of the active ingredient. They are clearly quite different objectives through different means.

Further, it is explained with Guittard's patent that the dispensing system includes a swellable hydrogel which extends in the inside of the tablet to occupy the whole space against the external wall. The external wall has to be perfored by means of a laser, in order to contact the layer of oxybutynin and to allow the penetration of digestive fluids into the formulation. More precisely, this kind of tablets is made of two layers, one of which including an osmotic agent and oxybutynin and the other layer is a contacting layer coated with a semi-permeable wall with pores which insure the diffusion of the active ingredient.

For these many reasons it has to be considered that the Guittard's patent discloses formulations which insure a long lasting release of the active ingredient while limiting to 20 to 30% the occurrence of the noxious des ethyl metabolite, whereas though the vaginal or rectal formulations, the formation of des ethyl derivative is reduced to about nothing. Therefore, the Guittard's patent discloses pharmaceutical composition intended only for the oral way producing a quick release of the active ingredient and biological effect which lasts from 4 to 6 hours. Moreover, the oral administration shows the occurrence of the des ethyl metabolite in significant amounts and for at least 12 hours. On the contrary, the administration of oxybutynin optionally associated to an estrogenic derivative, though the vaginal

or rectal routes leads to different pathways of metabolism avoiding the oxidative desethylation in the liver and this allows new and unexpected therapeutic effects. Therefore, withdrawal of this ground of rejection is requested.

In view of the amendment to the claims, the new drawings and the above remarks, it is believed that the claims point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,

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Enclosures